Supplemental Material

Appendix

The International Collaboration of Comprehensive Physiologic Assessment Investigators

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Table S1. Characteristics of Patients According to the Registries.

	Total population	Korea registry	Japan registry	Spain registry
Per-patient analysis	**n=1,245**	**n=552**	**n=631**	**n=62**
General characteristics				
Age, years	64.7 ± 10.3	61.6 ± 10.3	67.4 ± 9.4	65.6 ± 10.8
Male	958 (76.9%)	389 (70.5%)	520 (82.4%)	49 (79.0%)
BMI, kg/m^2	24.8 ± 3.5	24.6 ± 3.0	24.8 ± 3.8	28.5 ± 4.4
Clinical presentation				
Stable ischemic heart disease	1115 (89.6%)	454 (88.2%)	631 (100%)	30 (48.4%)
Acute coronary syndrome	130 (10.4%)	98 (17.8%)	0 (0%)	32 (51.6%)
Cardiovascular risk factors				
Hypertension	817 (65.6%)	328 (59.4%)	444 (70.4%)	45 (72.6%)
Diabetes mellitus	445 (35.7%)	160 (29.0%)	260 (41.2%)	25 (40.3%)
Hypercholesterolemia	784 (63.0%)	350 (63.4%)	400 (63.4%)	34 (54.8%)
Current smoker	266 (21.4%)	105 (19.0%)	142 (22.5%)	19 (30.6%)
Obesity (BMI>25 kg/m^2)	548 (44.8%)	234 (42.7%)	280 (44.4%)	34 (79.1%)
Multivessel disease	435 (34.9%)	273 (49.5%)	113 (17.9%)	49 (79.0%)
Per-vessel analysis	**n=1,484**	**n=772**	**n=631**	**n=81**
Vessel location				
LAD	950 (64.0%)	463 (60.0%)	442 (70.1%)	45 (55.6%)
LCX	219 (14.8%)	136 (17.6%)	67 (10.6%)	16 (19.7%)

RCA	315 (21.2%)	173 (22.4%)	122 (19.3%)	20 (24.7%)
Target vessel PCI performed	464 (31.3%)	96 (12.4%)	338 (53.6%)	30 (37.0%)
Angiographic characteristics				
Reference diameter	2.9 ± 0.6	3.0 ± 0.6	2.8 ± 0.7	2.8 ± 0.7
Diameter stenosis, %	46.0 ± 16.8	42.5 ± 17.5	49.7 ± 15.2	53.2 ± 12.5
Lesion length, mm	12.6 ± 8.6	11.6 ± 8.3	12.6 ± 7.5	23.0 ± 13.0
Physiologic parameters				
Resting Pd/Pa	0.93 ± 0.08	0.95 ± 0.06	0.90 ± 0.09	0.89 ± 0.09
Fractional flow reserve	0.83 ± 0.11	0.86 ± 0.10	0.79 ± 0.11	0.80 ± 0.10
Coronary flow reserve	2.9 ± 1.3	3.1 ± 1.3	2.8 ± 1.3	2.1 ± 1.4
IMR, U	21.0 ± 13.9	19.4 ± 9.7	22.9 ± 17.1	20.9 ± 18.5
Resistive reserve ratio	3.7 ± 1.7	3.8 ± 1.6	3.6 ± 1.7	2.7 ± 1.9

Values expressed as mean ± SD or number (%).

BMI, body mass index; IMR, index of microcirculatory resistance; LAD, left anterior descending artery; LCX, left circumflex artery; Pa, aortic pressure; Pd, distal coronary pressure; RCA, right coronary artery; Tmn, mean transit time.

Table S2. Characteristics of Patients with Deferred Revascularization According to Resistive Reserve Ratio in High CFR or High FFR Subgroups.

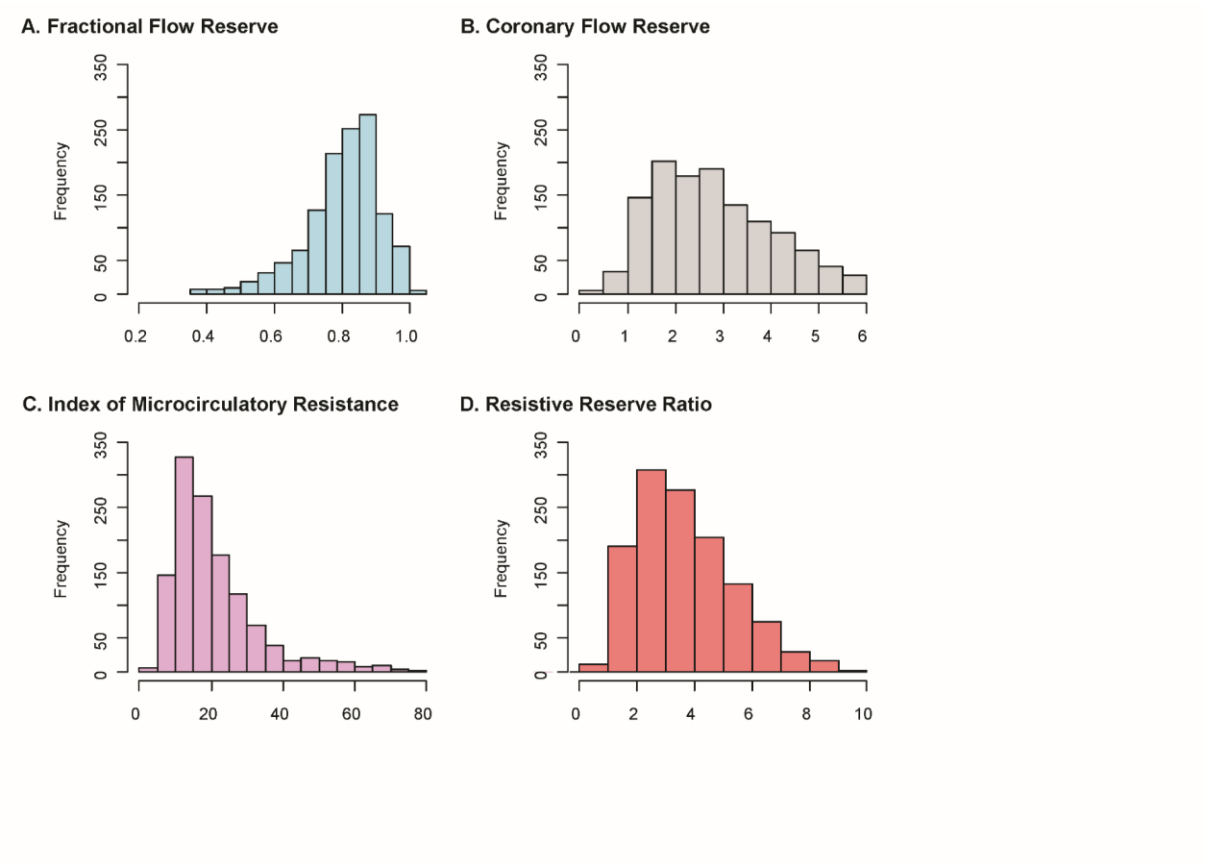
	High FFR Population			High CFR Population		
	RRR≥3.5	**RRR<3.5**	**P value**	**RRR≥3.5**	**RRR<3.5**	**P value**
Per-patient analysis (n=787)	**349/643 (54.3%)**	**294/643 (45.7%)**		**416/597 (69.7%)**	**181/597 (30.3%)**	
General characteristics						
Age, years	62.4 ± 10.5	65.8 ± 10.0	<0.001	62.3 ± 10.3	65.0 ± 10.2	0.003
Male	268 (76.8%)	193 (65.7%)	0.002	331 (79.6%)	118 (65.2%)	<0.001
BMI, kg/m^2	24.8 ± 3.9	24.7 ± 3.5	0.911	24.9 ± 3.8	24.6 ± 3.5	0.476
Clinical presentation			**0.827**			**1.000**
Stable ischemic heart disease	308 (88.2%)	262 (89.1%)		366 (88.0%)	159 (87.9%)	
Acute coronary syndrome	41 (11.8%)	32 (10.9%)		50 (12.0%)	22 (12.1%)	
Cardiovascular risk factors						
Hypertension	213 (61.0%)	187 (63.6%)	0.556	262 (63.0%)	109 (60.2%)	0.584
Diabetes mellitus	99 (28.4%)	115 (39.1%)	0.005	114 (27.4%)	74 (40.9%)	0.002
Hypercholesterolemia	219 (62.8%)	170 (57.8%)	0.233	263 (63.2%)	114 (63.0%)	1.000
Current smoker	74 (21.2%)	64 (21.8%)	0.938	87 (20.9%)	41 (22.7%)	0.713
Obesity (BMI>25 kg/m^2)	154 (44.4%)	126 (43.9%)	0.968	189 (45.8%)	79 (44.9%)	0.916
Multivessel disease	120 (34.4%)	129 (43.9%)	0.017	155 (37.3%)	73 (40.3%)	0.536
Per-vessel analysis (n=1,020)	**470/866 (54.3%)**	**396/866 (45.7%)**		**540/767 (70.4%)**	**227/767 (29.6%)**	
Vessel location			**0.071**			**0.132**

LAD	261 (55.5%)	231 (58.3%)		324 (60.0%)	144 (63.4%)	
LCX	77 (16.4%)	79 (20.0%)		79 (14.6%)	40 (17.6%)	
RCA	132 (28.1%)	86 (21.7%)		137 (25.4%)	43 (18.9%)	
Angiographic characteristics						
Reference diameter	3.1 ± 0.6	2.9 ± 0.6	0.001	3.0 ± 0.6	2.9 ± 0.7	0.007
Diameter stenosis, %	39.0 ± 14.9	39.6 ± 14.8	0.501	40.2 ± 15.0	39.9 ± 14.6	0.789
Lesion length, mm	10.9 ± 7.0	10.9 ± 6.9	0.988	11.3 ± 7.6	10.5 ± 6.3	0.126
Physiologic parameters						
Resting Pd/Pa	0.96 ± 0.04	0.96 ± 0.04	<0.001	0.96 ± 0.04	0.95 ± 0.04	0.141
Fractional flow reserve	0.90 ± 0.05	0.90 ± 0.05	0.757	0.88 ± 0.07	0.88 ± 0.07	0.383
Coronary flow reserve	4.1 ± 0.9	2.0 ± 0.6	<0.001	4.0 ± 0.9	2.5 ± 0.3	<0.001
Resting Tmn, sec	0.99 ± 0.44	0.62 ± 0.40	<0.001	0.98 ± 0.43	0.72 ± 0.38	<0.001
Hyperemic Tmn, sec	0.25 ± 0.11	0.31 ± 0.21	<0.001	0.25 ± 0.11	0.29 ± 0.16	<0.001
IMR, U	18.9 ± 8.7	24.0 ± 18.3	<0.001	18.3 ± 8.5	22.3 ± 12.8	<0.001
Resistive reserve ratio	5.1 ± 1.2	2.4 ± 0.7	<0.001	5.1 ± 1.2	3.0 ± 0.3	<0.001

Values expressed as mean ± SD or number (%).

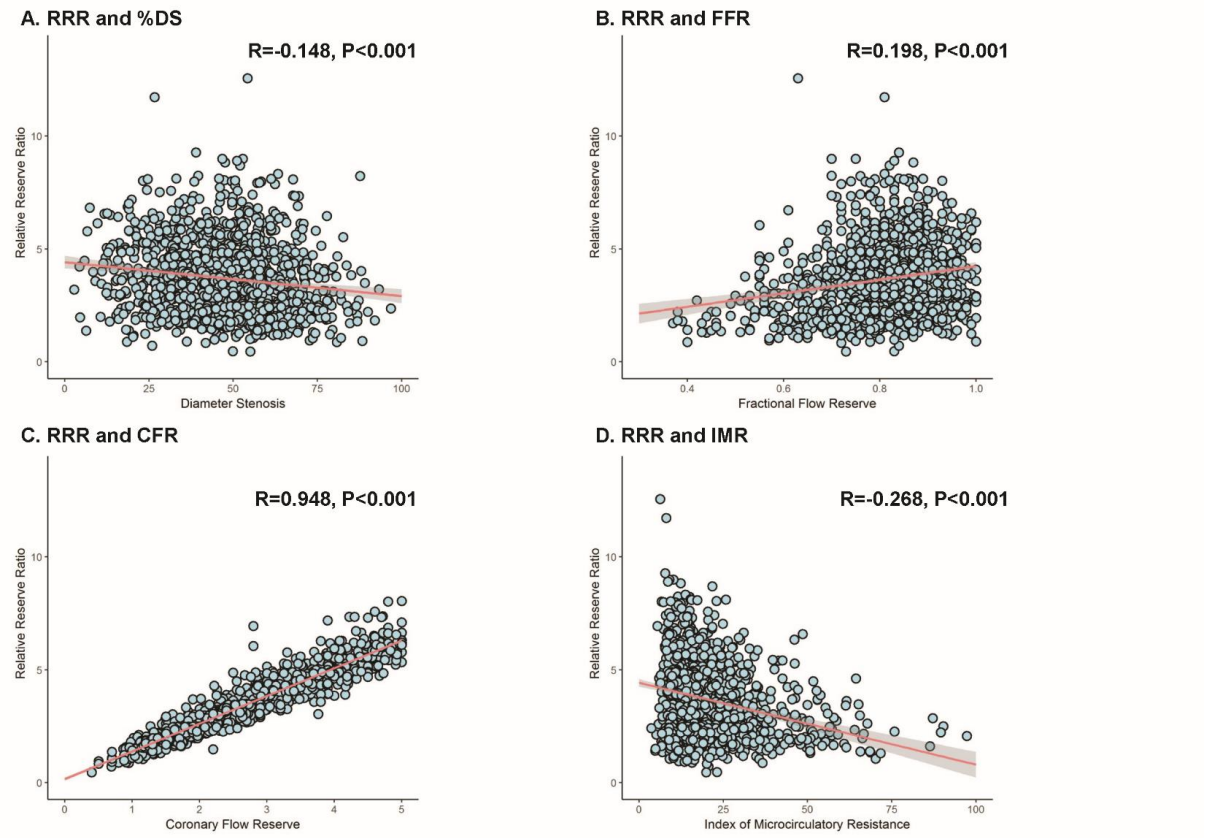
BMI, body mass index; IMR, index of microcirculatory resistance; LAD, left anterior descending artery; LCX, left circumflex artery; Pa, aortic pressure; Pd, distal coronary pressure; RCA, right coronary artery; RRR, resistive reserve ratio; Tmn, mean transit time.

Figure S1. Distribution of Physiologic Indices.



Distributions of (A) fractional flow reserve, (B) coronary flow reserve, (C) index of microcirculatory resistance, (D) resistive reserve ratio are shown.

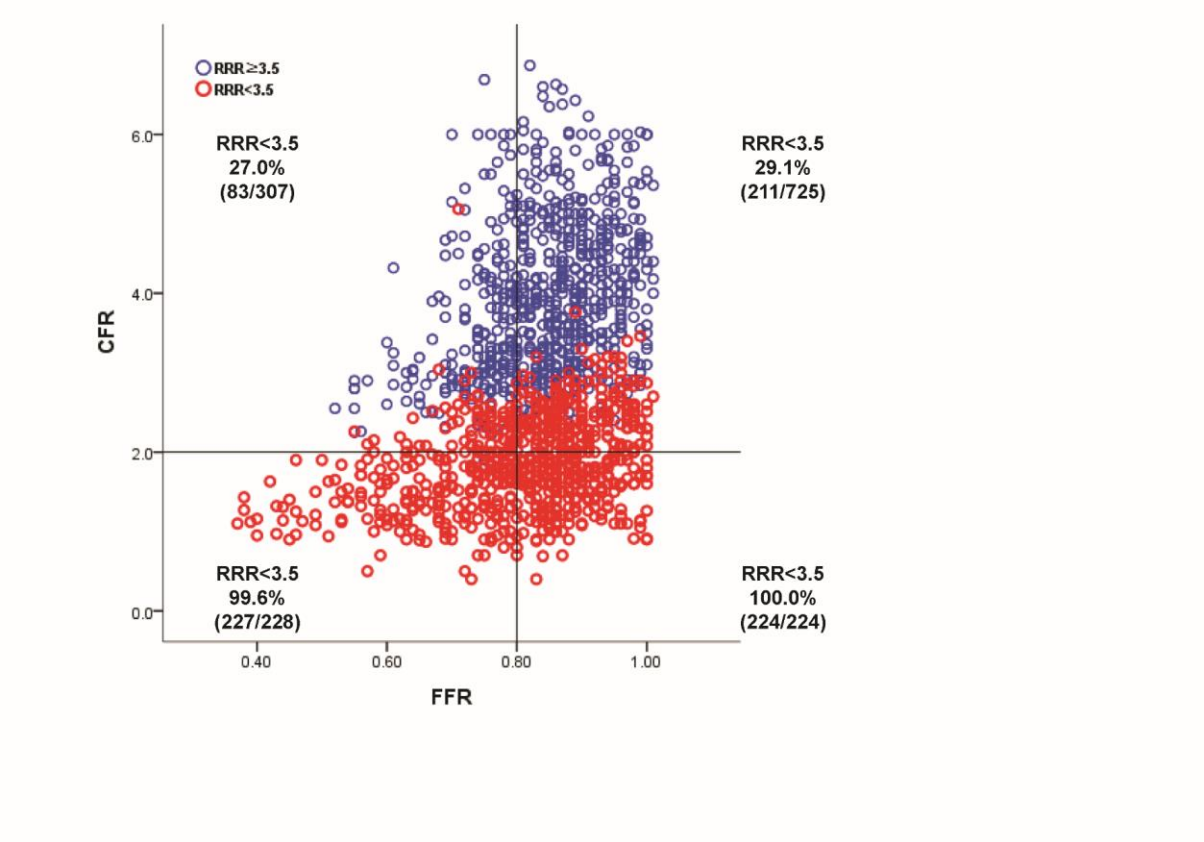
Figure S2. Correlation of Resistive Reserve Ratio with Diameter Stenosis or Other Physiologic Indices.



Correlation of RRR with **(A)** percent diameter stenosis, **(B)** FFR, **(C)** CFR, and **(D)** IMR.

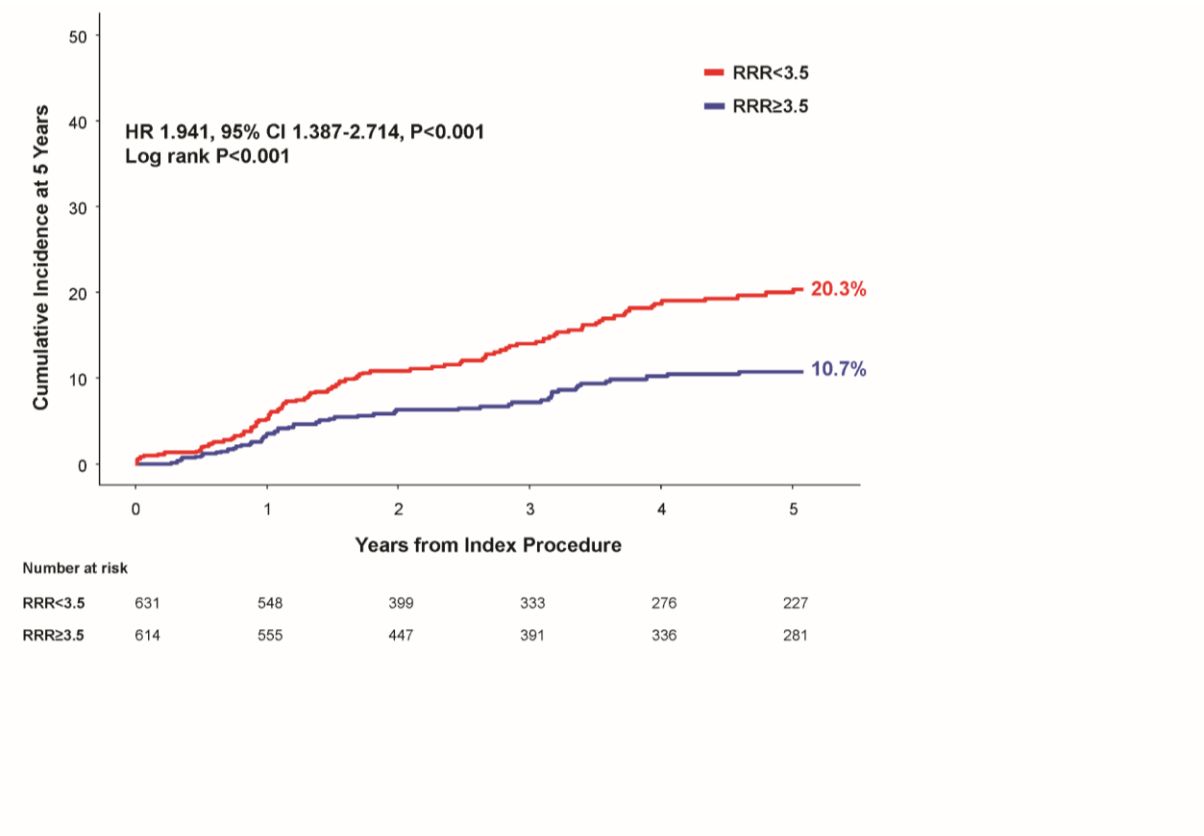
CFR, coronary flow reserve; FFR, fractional flow reserve; IMR, index of microcirculatory resistance; %DS, percent diameter stenosis; RRR, resistive reserve ratio.

Figure S3. Distribution of CFR, FFR and Resistive Reserve Ratio.



Distribution of vessels according to CFR and FFR values. Red dots represented vessels with depressed resistive reserve ratio (RRR) <3.5 and blue dots represent those with preserved RRR≥3.5. Although RRR showed high correlation with CFR (R=0.948, p<0.001), the classification agreement between CFR and RRR was only modest (Kappa value 0.605, p<0.001) and 28.6% of patients with CFR>2.0 showed low RRR (<3.5). Numbers represent the number of vessels in each quadrant.

Figure S4. Comparison of Patient-Oriented Composite Outcome According to Resistive Reserve Ratio.



Cumulative incidence of patient-oriented composite outcomes (POCO) is shown according to cut-off value of resistive reserve ratio (RRR). Unadjusted hazard ratio and 95% confidence intervals are presented._CI, confidence intervals; HR, hazard ratios; RRR, resistive reserve ratio.